

-continued

&lt;400&gt; SEQUENCE: 100

Arg Val Thr Ser Pro Asn Ile Thr Val Thr Leu Lys  
 1 5 10

&lt;210&gt; SEQ ID NO 101

&lt;211&gt; LENGTH: 11

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

&lt;220&gt; FEATURE:

&lt;221&gt; NAME/KEY: MISC\_FEATURE

&lt;222&gt; LOCATION: (1)..(1)

&lt;223&gt; OTHER INFORMATION: May or may not be present

&lt;400&gt; SEQUENCE: 101

Lys Gly Phe Ile Ile Ser Asn Ala Thr Tyr Lys  
 1 5 10

&lt;210&gt; SEQ ID NO 102

&lt;211&gt; LENGTH: 9

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

&lt;220&gt; FEATURE:

&lt;221&gt; NAME/KEY: MISC\_FEATURE

&lt;222&gt; LOCATION: (1)..(1)

&lt;223&gt; OTHER INFORMATION: May or may not be present

&lt;400&gt; SEQUENCE: 102

Lys Leu Val Leu Asn Cys Thr Ala Arg  
 1 5

&lt;210&gt; SEQ ID NO 103

&lt;211&gt; LENGTH: 7

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Artificial Sequence

&lt;220&gt; FEATURE:

&lt;223&gt; OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide

&lt;220&gt; FEATURE:

&lt;221&gt; NAME/KEY: MISC\_FEATURE

&lt;222&gt; LOCATION: (1)..(1)

&lt;223&gt; OTHER INFORMATION: May or may not be present

&lt;400&gt; SEQUENCE: 103

Lys Asn Ser Thr Phe Val Arg  
 1 5

1. A method of producing an aflibercept composition having a target value of aflibercept variants expressed in a host cell cultured in a chemically defined medium (CDM), comprising:

- (a) providing said host cell genetically engineered to express aflibercept;
- (b) culturing said host cell in said CDM under suitable conditions in which said host cell expresses aflibercept to produce an aflibercept sample;
- (c) clarifying and harvesting the aflibercept sample produced by said host cell, wherein the target value of aflibercept variants is obtained by using:

- i. a cumulative concentration of iron in said CDM of less than or equal to about 55.0  $\mu\text{M}$ ;
- ii. a cumulative concentration of copper in said CDM of less than or equal to about 0-8  $\mu\text{M}$ ;
- iii. a cumulative concentration of nickel in said CDM of less than or equal to about 0.4  $\mu\text{M}$ ;
- iv. a cumulative concentration of zinc in said CDM of less than or equal to about 56.0  $\mu\text{M}$ ;
- v. a cumulative concentration of cysteine in said CDM of less than or equal to about 10.0 mM; and/or
- vi. cumulative concentration of an anti-oxidant in the CDM of about 0.001 mM to about 10 mM for any